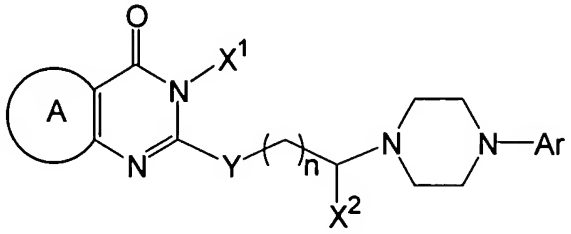
CLAIMS

1. Pyrimidine derivatives represented by the following formula (I)



(I)

in which

ring A stands for a carbocyclic group or heterocyclic group,

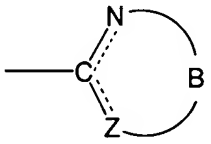
X^1 stands for hydrogen, amino, lower alkylamino, di-lower alkylamino, lower alkylideneamino, lower alkyl, phenyl lower alkyl or substituted or unsubstituted phenyl,

X^2 stands for hydrogen or lower alkyl,

Y stands for a direct bond, sulfur or nitrogen,

n is 0 or an integer of 1 – 4,

Ar stands for a group represented by the following formula,



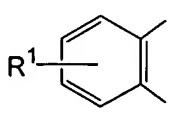
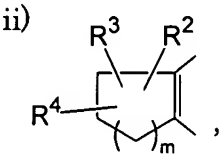
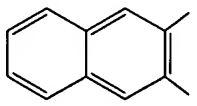
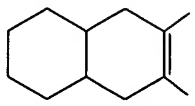
which is either unsubstituted or substituted with substituent(s) selected from halogen, lower alkyl, hydroxyl, lower alkoxy and phenyl, and in which

Z stands for carbon, oxygen or sulfur,

B stands for the residual member(s) necessary for completing a monocyclic or polycyclic, nitrogen-containing heterocyclic group, which may form a condensed ring together with the remainder of the group of the above formula, and the dotted lines indicate optionally existing bonds,

or their pharmaceutically acceptable salts.

2. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 1, in which the ring A stands for a carbocyclic group represented by any of the following formulae i) – iv):

i)  ii)  iii)  iv) 

in which

R^1 stands for hydrogen, halogen, lower alkyl, halogenated lower alkyl, lower alkoxy, carboxyl, lower alkoxycarbonyl, phenyl, amino, hydrazino or nitro,

R^2, R^3 and R^4 either stand for, independently from each other, hydrogen, halogen, lower alkyl, lower alkoxy, phenyl or hydroxyl; or two out of R^2, R^3 and R^4 together stand for oxo or lower alkylenedioxy, and

m is an integer of 1 – 3.

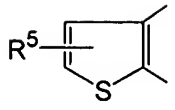
3. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 2, in which the ring A stands for a carbocyclic group represented by the formula ii).

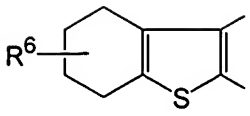
4. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 3, in which m is 2.

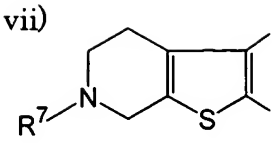
5. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 4, in which all of R^2, R^3 and R^4 stand for hydrogen atoms.

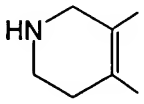
6. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 1, in which the ring A stands for a heterocyclic group represented by any of the following formulae v) –

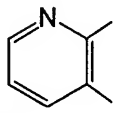
xv):

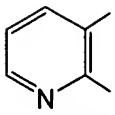
v)  ,

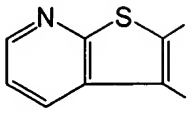
vi)  ,

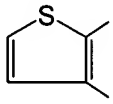
vii)  ,

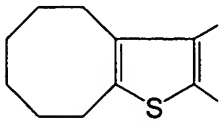
viii)  ,

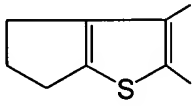
ix)  ,

x)  ,

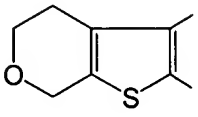
xi)  ,

xii)  ,

xiii)  ,

xiv)  ,

and

xv) 

in which

R^5 stands for hydrogen, lower alkyl, carboxyl or lower alkoxycarbonyl,

R^6 stands for hydrogen or lower alkyl,

and

R^7 stands for hydrogen, lower alkyl, lower alkanoyl, lower alkoxycarbonyl or phenyl lower alkoxycarbonyl.

7. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in any one of Claims 1 –6, in which X^1 stands for hydrogen, amino or lower alkyl.

8. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 7, in which X^1 stands for amino or lower alkyl.

9. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in any one of Claims 1 –8, in which X^2 stands for hydrogen.

10. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in any one of Claims 1 –9, in which Y stands for a direct bond or sulfur.

11. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in any one of Claims 1 –10, in which n stands for 2 or 3.

12. The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in any one of Claims 1 – 11, in which Ar stands for quinolyl group which is either unsubstituted or substituted with substituent(s) selected from halogen, lower alkyl, hydroxyl, lower alkoxy and phenyl.

13. A pyrimidine derivative selected from the group consisting of the following compounds or pharmaceutically acceptable salt thereof: 3-amino-5,6-dimethyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-3H-thieno[2,3-d]pyrimidin-4-one,
3-amino-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one,
3-amino-5,6-dimethyl-2-[3-(4-pyrrolo[1,2-a]quinoxalin-4-ylpiperazin-1-yl)propylthio]-3H-thieno[2,3-d]pyrimidin-4-one,
3-amino-5-methyl-4-oxo-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]- 3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxylic acid ethyl ester,
3-amino-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-5,6,7,8,9,10-hexahydro-3H-11-thia-1,3-diazacycloocta[a]inden-4-one,
3-amino-7-methyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one,
3-amino-2-[3-[4-(4-methylquinolin-2-yl)piperazin-1-yl]propylthio]-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one,
3-amino-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-5,6,7,8-tetrahydro-3H-9-thia-1,3,7-triazafluoren-4-one,
5,6-dimethyl-2-[3-(4-pyridin-2-ylpiperazin-1-yl]propylthio]-3H-thieno[2,3-d]pyrimidin-4-one,

2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-3H-thieno[3,2-d]pyrimidin-4-one,
6-propyl-2-[3-(4-quinolin-2-yl-piperazin-1-yl)propylthio]-3H-pyrimidin-4-one,
2-[3-[4-(4-methylquinolin-2-yl)piperazin-1-yl]propylthio]-5,6,7,8-tetrahydro-3H-9-thia-1,3,7-triazafluoren-4-one,
5,6-dimethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-thieno[2,3-d]pyrimidin-4-one,
2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-9-thia-1,3,7-trazafluoren-4-one,
3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,
3-amino-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-3H-quinazolin-4-one,
3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-thieno[3,2-d]pyrimidin-4-one,
3-amino-6-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,
3-amino-2-[4-[4-(5-methoxyquinolin-2-yl)piperazin-1-yl]butyl]-3H-quinazolin-4-one,
3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-thieno[2,3-d]pyrimidin-4-one,
3-amino-5-chloro-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,
3-amino-5-hydrazino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,
3-amino-5,6-dimethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-thieno[2,3-d]pyrimidin-4-one,
3-amino-8-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3,5,6,7,8,9-hexahydro-cyclohepta[d]pyrimidin-4-one,
3-amino-6-fluoro-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-

quinazolin-4-one,
3-amino-6-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-amino-6-ethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-amino-6-hydroxy-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylamino]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
2-[3-[4-(4-methylquinolin-2-yl)piperazin-1-yl]propylamino]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylamino]-3H-pyrimidin-4-one,
2-[3-(4-pyrrolo[1,2-a]quinoxalin-4-ylpiperazin-1-yl)propylamino]-3H-quinazolin-4-one,
3-amino-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylamine]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-ethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-methyl-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-ethyl-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-benzyl-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,
3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,
3-ethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,
6-chloro-3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,
3-methyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-5,6,7,8-tetrahydro-3H-quinazolin-4-one, and
3-methyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-3H-

quinazolin-4-one.

14. Serotonin receptor subtype 3 (5-HT_3) antagonistic agents concurrently having serotonin receptor subtype 1A (5-HT_{1A}) agonistic activity, characterized by containing the pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in any one of Claims 1 – 13.

15. Medical compositions containing the pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in any one of Claims 1 – 13 and pharmaceutically acceptable carriers.

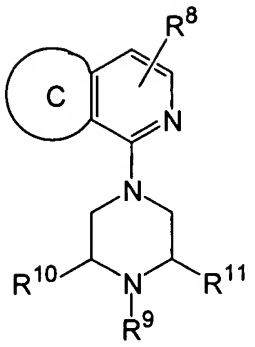
16. Treating agents for irritable bowel syndrome (IBS), functional dyspepsia (FD), anxiety, urinary incontinence, anischuria, depression, prostate cancer, asyndesis, pollakiuria, schizophrenia, overactive bladder syndrome, psychosis, lower urinary tract symptom, senile dementia, bladder outlet obstruction associated with benign prostatic hyperplasia, Alzheimer disease, interstitial cystitis, addiction/withdrawal symptom, chronic prostatitis, cognitive impairment, acute ischemic stroke, Huntington's disease, transient ischemic attack, Parkinson's disease, head or spinal cord trauma, amyotrophic lateral sclerosis, fetal hypoxemia, AIDS dementia complex, nonulcer dyspepsia, chronic neurodegenerative disease, for example, retinal disease, reflux esophagitis, alcohol or cocaine addiction, hypersensitive bowel syndrome, extrapyramidal disorder, apnea/hypopnea syndrome, panic disorder, tremor, disturbance of short-term memory, nausea or emesis, alcoholism, epilepsy, nicotine dependence, sleep disorder, drug addiction, pain, eating disorder, sexual dysfunction, posttraumatic stress disorder, obesity, autism, cough, nerve root compression syndrome, myofascial syndrome, neuropathy, tendomyosis, algetic dystrophy, tendinosis, agitation, tendopathy, hostility, synovial bursa related disease, obsessive-compulsive disorder, periarthropathy, cognition enhancement, myofascial pain syndrome, premenstrual tension syndrome, autonomic imbalance, essential hypertension,

psychophysiologic disorder, convulsion, peptic ulcer, mania, gastritis, migraine, meniscal lesion, polyarthritis, traumatic arthritis, paraneoplastic syndrome, osteochondritis dissecans, tumor-elicited inflammatory disease, osteonecrosis, inflammatory exudation, articularis chondromatosis, connective tissue disease, chronic obstructive pulmonary disease (COPD), infectious arthritis, acute respiratory distress syndrome (ARDS), seronegative spondyloarthropathy, bronchitis, vasculitis, pneumoconiosis, sarcoid arthropathy, laryngospasm, pulmonary angiitis, pulmonary granuloma, extrinsic allergic alveolitis, chronic fatigue syndrome, contact hypersensitivity and glaucoma, characterized by containing the pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in any one of Claims 1 – 13.

17. A therapeutic method of irritable bowl syndrome (IBS) characterized by exerting 5-HT_{1A} agonistic activity and 5-HT_3 antagonistic activity in vivo simultaneously and cooperatively, which comprises administering to human being or other mammals who require irritable bowel syndrome (IBS) therapy, 5-HT_3 antagonistic agent which concurrently exhibits 5-HT_{1A} agonistic activity, or administering 5-HT_{1A} agonistic agent and 5-HT_3 antagonistic agent simultaneously, or in sequence, or at an interval.

18. The method as set forth in Claim 17, in which the 5-HT_3 antagonistic agent concurrently having 5-HT_{1A} agonistic activity is a pyrimidine derivative or a pharmaceutically acceptable salt thereof as set forth in Claim 1.

19. The method as set forth in Claim 17, in which the 5-HT_3 antagonistic agents concurrently having 5-HT_{1A} agonistic activity are piperazinylpyridine derivatives represented by the following formula (II),



(II)

in which

ring C stands for unsubstituted benzene ring or an unsubstituted heterocyclic group selected from pyridine, furan and thiophene; benzene ring substituted with substituent(s) selected from halogen, lower alkyl, phenyl, hydroxyl, lower alkoxy, phenyl lower alkoxy (the phenyl moiety being either unsubstituted or halogen-substituted), amino, lower alkylamino, di-lower alkylamino, lower alkylthio, lower alkylsulfinyl and aminosulfonyloxy; or heterocyclic group selected from halogen- or lower alkyl-substituted pyridine, furan and thiophene,

R^8 stands for hydrogen, halogen or lower alkyl,

R^9 stands for hydrogen, lower alkyl, phenyl lower alkyl (the phenyl moiety being unsubstituted or substituted with substituent(s) selected from halogen, lower alkyl and lower alkoxy), amino lower alkyl (the amino moiety being either unsubstituted or mono- or di-substituted with lower alkyl, or optionally forming a cyclic imido group) or phenyl cycloalkyl (the phenyl moiety being either unsubstituted or substituted with substituent(s) selected from halogen, lower alkyl and lower alkoxy),

R^{10} stands for hydrogen or lower alkyl, or

R^9 and R^{10} may together form the residual members of pyrrolidine ring or piperidine ring (which may be unsubstituted or substituted with substituent(s) selected from hydroxyl, lower alkoxy and phenyl lower alkoxy), and

R^{11} stands for hydrogen or lower alkyl,

or their pharmaceutically acceptable salts.

20. The method as set forth in Claim 19, in which the 5-HT_3 antagonistic agents concurrently having 5-HT_{1A} agonistic activity are piperazinylpyridine derivatives selected from the group consisting of the following compounds, or their pharmaceutically acceptable salts:

7-chloro-1-(4-methylpiperazin-1-yl)isoquinoline,

7-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)thieno[2,3-c]-pyridine,

7-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)furo[2,3-c]-pyridine,

2-methyl-4-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)-thieno[3,2-c]pyridine,

7-methoxy-1-((8aR)-octahydropyrrolo[1,2-a]pyrazin-2-yl)-isoquinoline,

and

2-bromo-4-(4-methylpiperazin-1-yl)thieno[3,2-c]pyridine.

21. The method as set forth in Claim 17, in which the 5-HT_{1A} agonistic agent is tandospirone, and 5-HT_3 antagonistic agent is a compound selected from alosetron, granisetron, azasetron, tropisetron, ramosetron, ondansetron, lerisetron, cilansetron, itasetron, indisetron, dolasetron and (R)-zacopride.

22. Combinations of medical preparations for treating irritable bowel syndrome, which comprise 5-HT_{1A} agonistic agent and 5-HT_3 antagonistic agent.